REMARKS

Claims 1-14, 16-38 constitute the pending claims in the present application. Issues raised by the Examiner will be addressed below in the order they appear in the prior Office Action. Applicants respectfully request reconsideration in view of the following remarks.

1. Applicants have added the phrase "boronyl peptidomimetic" before the term "inhibitor" in claim 29.

2. Applicants have herein corrected the misspelling of the term "organics" on page 9, line 6 of the specification.

3. Claims 2-4, 6-14, 16-23, 28, and 31-37 are rejected under 35 U.S.C. 112, second paragraph.

a. Claims 2-4 are deemed indefinite because they do not explicitly recite what constitutes Formula 1. Applicants have herein explicitly defined Formula 1 for claims 2-4. Applicants assert that the amendments do not narrow the scope of the claims.

b. Applicants have removed the term "including" from claims 16, 28 and 31. Applicants assert that the amendments do not narrow the scope of the claims.

c. Applicants corrected the structural formula in claim 28. Applicants submit that the previous structure was an obvious error, that one skilled in the art would have recognized that the structure as amended was what was intended in the first place. Applicants respectfully submit that the amended structure renders moot the concerns raised in the Office Action.

d. Applicants have herein corrected the dependency of claim 31. Applicants assert that the amendment does not narrow the scope of the claim.

e. Applicants have removed variables R_5 and R_{61} from claim 31. Applicants assert that the amendment does not narrow the scope of the claim.

f. Applicants removal of the variable R_5 from Claim 31 renders moot the need to define R'_7.

g. Applicants have herein defined variable R_{62} for claim 31. Applicants assert that the amendment in no way narrows the scope of the claim.

h. Applicants have changed the term "and" to "or" in claim 37. Applicants assert that the amendment in no way narrows the scope of the claim.

Applicants appreciate the Examiner pointing out the informalities which Applicants have corrected above. Applicants assert that the claims are definite as amended. Applicants also assert that a skilled artisan would have recognized the informalities and the required corrections. As such, submit that a skilled artisan would not have been confused as to the scope of the claims.

5. Claims 1-14, 16-26, 28, and 30-36 are objected to for containing informalities. Applicants address each informality in the order that it is presented in the Office Action.

a. Applicants have herein removed the underlining on claim 1 of the amendment filed September 16, 2002. Applicants assert that the amendment does not narrow the scope of the claim.

b. Applicants have herein removed "or" from claim 1, page 6, line 10, of the amendment filed September 16, 2002. Applicants assert that the amendment does not narrow the scope of the claim.

c. Applicants have herein added a period at the end of claim 9. Applicants assert that the amendment does not narrow the scope of the claim.

d. Applicants have herein inserted an "or" at claim 24, page 11, line 9; claim 25, page 12, line 9, claim 26, page 13, line 10; claim 28, page 16, line 4; and claim 31, page 19, line 7. Applicants assert that the amendments do not narrow the scope of the claims.

e. Applicants have herein changed first occurrence of "a" to "an" at claim 24, page 11, line 12. Applicants assert that the amendment does not narrow the scope of the claim.

f. Applicants have herein inserted a semicolon at the end of the line at claim 28, page 17, line 8. Applicants assert that the amendment does not narrow the scope of the claim.

g. Applicants have herein inserted an "a" after "including" at claim 30, line 2. Applicants assert that the amendment does not narrow the scope of the claim.

h. Applicants have herein inserted an "or" before "hyperlipoproteinemia" at claim 32, line 2. Applicants assert that the amendment does not narrow the scope of the claim.

Applicants appreciate the Examiner pointing out the informalities which Applicants have corrected above. Applicants also assert that a skilled artisan would have recognized the informalities and the required corrections. As such, submit that a skilled artisan would not have been confused as to the scope of the claims.

6. Claim 26 is objected to under 37 C.F.R. 1.75(c) as being of improper dependency. Applicants have amended the claim to remove hydrogen from the definition of X_1 in claim 26. Applicants submit that the amended claim is of proper dependent form. Accordingly, Applicants respectfully request removal of the rejection.

7. Claims 1-14 and 16-37 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-67 of co-pending Application No. 09/628,225. The Office Action further stated that "[A]lthough the conflicting claims are not identical, they are not patently distinct from each other because the claims of the '225 application anticipate the instant claims." Applicants traverse the rejection to the extent it is maintained over the amendments. Applicants will address the issue at a later time, should it be maintained.

8. Applicants note with appreciation that rejections based on the Deacon et al. and WO Patent Application 98/25644 have been removed on account of the priority data of the instant application.

9. Claims 1-3, 5-13, 16, 20, 21, 25, and 29 are rejected under 35 U.S.C. 102(b) as being anticipated by the WO Patent Application '309. Applicants respectfully traverse the rejection.

Claims 1-4, and 29 are the independent claims in the rejected claim set. Claims 5-13, 16, 20, 21, and 25 ultimately depend from claims 1, 2, 3, or 4. Thus, if claims 1-4 are shown to be novel, then novelty inheres to the dependent claims.

Applicants reiterate their arguments from the previous response. Applicants assert that the instant claims are not anticipated by the '309 application. While the '309 application claims DPIV inhibitors, it does not disclose every element of the amended pending claims. The '309 application discloses that inhibition of DPIV inhibitors may be useful as immunosuppresants, prevention drugs for HIV infection of $CD4^+$ T-cells, preventions drugs for progression metastaeses, for treating psoriatic or arthritic conditions, for treating prostate hypertrophy, or for suppression of sperm motility. (See page 3 of '309 app) Thus, the '309 application does not teach or suggest that DPIV inhibitors can be used to modify glucose tolerance and/or GLP-1 metabolism in vivo, nor does the Examiner point to facts in the art that would bridge that gap. As such the instant claims are directed to new and unobvious uses of DPIV inhibitors not disclosed in the 309 application.

Applicants further reiterate their arguments regarding In re Marshall. The fact that glucose tolerance and/or GLP-1 metabolism might have been modified to the same extent in the experiments described in the '309 application is not relevant because, for inherent anticipation of **method claims**, if a claimed method comprises steps identical to those of a method practiced in the prior art, and the same result would have been achieved in the prior art method, the accidental or unwitting achievement of that result cannot constitute anticipation. *In re Marshall*, 578 F.2d 301, 198 USPQ 344 (CCPA 1978). In *Marshall* the PTO board used the *Physician's Desk Reference* (PDR) as a basis for a rejection of the applicant's weight control process. The applicant's process involved anesthetizing certain intestinal nerve ends receptors with oxethazaine. The anesthesia inhibited the release of certain appetite simulating hormones thereby inhibiting appetite. The PDR had disclosed that oxethazaine inhibits the release of gastrointestinal hormones, and such inhibition would be useful for treating certain gastrointestinal ailments. In reversing the Board's rejection, the court held that the PDR did not teach the use of the compound as a weight control drug. Addressing the issue of inherency, the court further stated that "[I]f anyone ever lost weight by following the PDR teachings it was an unrecognized accident. An accidental or unwitting duplication of an invention cannot constitute an anticipation." (*id.* 304)

Applicants maintain that *Marshall* is controlling in the instant situation. In *Marshall*, note that the essential question with regards to inherency was not whether oxethazaine had inhibited

the release of intestinal hormones in patients prior to the applicant's weight control process, or whether patients had lost weight when oxethazaine was administered to them as an anesthetic. Rather the question was whether the prior reference taught the reader that weight loss can be achieved by using oxathazine. Thus, if the 102 reference does not teach or suggest the claimed process, then the claimed process is new and unobvious in view of the reference.

The instant claims, as amended, are directed to uses of DPIV inhibitors to improve glucose tolerance and/or decrease GLP-1 metabolism in an animal. Applicants point out that the MPEP does not foreclose patentability where "new and unobvious uses of old structures and compositions" are present (MPEP 2112.02, original emphasis) Under *Marshall*, "accidental or unwitting duplication of an invention cannot constitute an anticipation." (*Marshall*, 578 F.2d at 304) Thus, to sustain an anticipation by inherency, the '309 application must teach or suggest the benefits of modifying GLP-1 metabolism in a manner that is not accidental or unwitting. One of ordinary skill in the art, having read the '309 application, should be able to achieve therapeutic benefits by modifying GLP-1 metabolism. The '309 application lists six pharmaceutical applications of the DPIV inhibitors discloses therein: (1) immunosuppression, (2) HIV prevention and AIDs treatment, (3) prevention of breast and prostate tumor metastases into the lungs, (4) treatment of dermatological diseases such as psoriasis, (5) suppression of sperm motility to achieve male contraception, and (6) treatment of benign prostate hypertrophy. (See '309 application, p. 3) Applicants point out that none of the six enumerated uses relate to glucose tolerance or GLP-1 metabolism. The '309 application was not seeking to improve glucose tolerance, it did not monitor the effects the DPIV inhibitors had on glucose tolerance, nor is there any suggestion that glucose tolerance was related to the therapeutic uses enumerated in the '309 application. To the best of Applicants' knowledge, GLP-1 is not related to the therapeutic uses enumerated in the '309 application. Applicants urge that one of ordinary skill in the art, having read the '309 application, would not have known to use DPIV inhibitors to improve glucose tolerance and/or decrease GLP-1 metabolism in vivo for therapeutic purposes.

The only biological testing carried out in the '309 application were *in vitro* assays using purified human DPIV. (See '309 application, page 9) There is no indication that any GLP-1 enzyme was even present in the preparation. The experiments disclosed in the '309 application neither show what effects the disclosed inhibitors had on glucose tolerance, nor do they show

any beneficial therapeutic uses arising from modifying GLP-1 metabolism. Applicants assert that one of ordinary skill in the art would have been hard pressed to find even a teaching or suggestion that the DPIV inhibitors could achieve beneficial uses by modifying GLP-1 metabolism. Thus, Applicants assert that an inherency rejection cannot be sustained based on the '309 application. Accordingly, Applicants respectfully request reconsideration and removal of the rejection.

The Office Action stated that *Marshall* does not represent the current state of the law with respect to inherency and anticipation rejections, and offered the following citations from the MPEP 2112 and 2112.02, *Ex parte Novitski*, 26 USPQ2d 1389, 1391 (BPAI 1993), *W.L. Gore & Assocs., Inc. v. Garlock, Inc.*, 721 F.2d 1540, 1548, 220 USPQ 303, 309 (Fed. Cir. 1983) cert. denied, 469 U.S. 851 (1984) and *Abbott Labs. v. Geneva Pharms., Inc.*, 182 F.3d 1315, 1319, 51 USPQ2d 1307, 1309 (Fed. Cir. 1999), cert. denied, 528 U.S. 1078 (2000). Applicants assert that the cases cited in the Office Action do not overrule *Marshall*, and are not in conflict with *Marshall*. Applicants assert that anticipation is a complex legal field encompassing on-sale bar, public use and various common law exceptions. New cases may arise to address different aspects of anticipation. Indeed, the cases cited by in the Office Action may reflect the efforts various courts to address aspects of anticipation. Applicants argue, however, the appearance of new cases which do not overrule or narrow the older cases, does not reduce the controlling force of the older cases. Applicants assert that Marshall is still good law even in view of the cases cited in the Office Action. The Federal Circuit in 1990 cited *Marshall* approvingly acknowledging patentability of method claims when an applicant discovers a completely new use for an old compound. (See *In re Woodruff*, 919 F.2d 1575, 1578) Moreover, the "accidental or unwitting duplication test" of *Marshall* has been applied as recently as 1998 in *Mehl/Biophile Int'l Corp v. Milgraum*, 8 F. Supp.2d 434, 447.

Applicants further assert that *Marshall* is not in conflict with the *Abbot* decision cited in the Office Action because the two opinions relate to anticipation in different contexts. The Office Action stated that under *Abbot Labs. v. Geneva Pharms., Inc.*, 182 F.3d 1315, the "accidental and unwitting cases" are only applicable when the claimed invention is "anticipated by earlier work that produced no useful or appreciated result." (See Abbot Labs, at 1319) Applicants assert that *Abbot* is not conflict with *Marshall*. Specifically, *Marshall* deals with anticipation in the

method claim context, while Abbot deals with anticipation in the **on-sale bar** context. This distinction is important because, *Abbot* did not involve a new use for an old compound. Applicants argue that the Fed. Cir. in *Abbot* did not mean to foreclose patentability of a claimed invention by an earlier work just because the earlier work produced something useful or appreciated regardless of whether elements of the claimed invention contributed to the usefulness of the product, or if what is appreciated about the product are the elements in the claimed invention. Such an interpretation would be problematic and inapposite with the language and understanding of MPEP 2112 and 2112.02 which does not foreclose patentability in cases where old structures and compositions are used in "new and unobvious uses." (See MPEP 2112.02) Rather, the Federal Circuit held that anticipation of a claimed invention would be sustained only when the useful and appreciated results of the earlier work are attributable to the elements disclosed in the claimed invention. In *Abbot* the court determined the sale of a batch crystalline polymorph one year prior to Abbot's patent application for one of the polymorphs posed an on-sale bar regardless of whether the seller or buyer knew that the product sold had the claimed characteristics. The court correctly found anticipation because the sold samples consisted of the claimed polymorph, the samples had pharmaceutical use, and the use was attributable to the claimed polymorph. Thus *Abbot* was not addressing an "accidental and unwitting" case within the *Marshall* context.

Whereas *Abbot* did not fall in the "accidental and unwitting" category, Applicants assert the instant situation falls squarely within *Marshall*. In the present case, the cited earlier work was directed to uses that are different than the claimed methods, i.e., the inventors assert that they are affecting a different biological process. The Office Action has not presented any evidence that the underlying success and usefulness of the earlier works is attributable to modification of GLP-1 metabolism in vivo. Thus the cited earlier works do not inherently anticipate the instant method claims.

10. Claims 1-3, 5-13, 16-24, 26, 27, 29-35 and 37 U.S.C. 102(b) as being anticipated by the WO Patent Application '259. Applicants traverse the rejection to the extent it is maintained over the amended claims.

Applicants reiterate their previous arguments. To anticipate a claim, the reference must teach every element of the claim. (MPEP 2131) While the '259 application makes composition of matter claims of DPIV inhibitors, it does not disclose every material element of the claimed subject matter of the instant application because it does not teach or suggest that DPIV inhibitors can be used to improve glucose tolerance or decrease GLP-1 metabolism in vivo. As above, If the Examiner continues to rely on rejecting the pending claims as being anticipated by the '259 application, Applicants respectfully request that the factual basis, including that which overcomes the mere anticipated inherency [if at all], be clearly articulated. Any modulation of GLP-1 metabolism in the experiments described in the '259 application would have been an unrecognized accident, and thus cannot constitute inherent anticipation of the instant claims. Therefore, Applicants respectfully request reconsideration of this rejection.

11. Claims 1-14, and 29 are rejected under 35 U.S.C. 102(e) as being anticipated by Villhauer. The Office action stated that "since the same active agents are being administered to the same animals according to the same method steps, inherently peptide hormone metabolism will be modified t the same extent in the method of Villhauer as is claimed by Applicants." Applicants respectfully traverse the rejection to the extent it is maintained over the amended claims.

Applicants assert that Villhauer does not disclose the compounds in the instant claims as amended. To anticipate a claim, the reference must teach every element of the claim. (MPEP 2131) Applicants have cancelled claim 15. To the extent the subject matter of claim 15 appears in other claims, namely claims 1-4, Applicants have amended the claims such that the compounds in the instant claims are not within the scope of the compounds disclosed by Villhauer. Note in particular that all of Villhauer's compounds contain a prolyl residue wherein the carboxyl moiety has been replaced by a cyano group. In amended claims 1-4 and claims dependent thereon, Applicants have removed a cyano group from being one of the possibilities for W. Therefore, Applicants assert that the compounds in the instant amended claims 1-4, and the claims dependent thereon, are not the same as Villhauer's compounds. Thus, Villhauer does not disclose all the limitations of the instant claims. Accordingly, Applicants respectfully request reconsideration and removal of the rejection.

21. Claims 29 is rejected under 35 U.S.C. 102(b) as being anticipated by the German Patent 19 61 6486. Applicants traverse the rejection to the extent it is maintained over the amended claims.

Applicants have amended claim 29 so that the claim is drawn to boronyl peptidomimetic inhibitors of dipeptidyl peptidase IV. Applicants assert that the '486 patent does not disclose boronyl peptidomimetic inhibitors of dipeptidyl peptidase IV. As such, Applicants submit that the '486 patent fails to anticipate 29 because it does not disclose every limitation of the claims. Therefore, Applicants respectfully request reconsideration and removal of the rejection.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants submit that the pending claims are in condition for allowance. Early and favorable reconsideration is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000. Should an extension of time be required, Applicants hereby petition for same and request that the extension fee and any other fee required for timely consideration of this submission be charged to **Deposit Account No. 18-1945.**

Respectfully Submitted,

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